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MUCORMYCOSIS - AN EPIDEMIC IN A PANDEMIC: A COMPLICATION OF COVID-19

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ABSTRACT: Mycosis is an opportunistic infection that attacks patients who are immunocompromised. Our immune system is designed to defend us against fungus and bacteria. The fungus can expand, penetrate and kill tissue because it lacks immunity. It's everywhere, in soil and air and even in healthy people's noses and snot, says the researcher. "As we work to defend ourselves from COVID-19 and live with it, another hazard termed Mucormycosis has emerged. Mucormycosis, a fungal infection caused by Mucor with a 50% fatality rate, maybe provoked by the administration of steroids, a life-saving treatment for severe and critically ill Covid-19 patients. Stay safe from Mucormycosis, a fungus that has been discovered in Covid-19 patients.

INTRODUCTION: Mucormycosis, also known as black fungus or Zygomycosis, is an uncommon but deadly fungal complication caused by a group of moulds known as mucormycetes, order Mucorales. It is caused by inhaling fungal spores in the environment. During or after recovery, a few COVID-19 patients have been documented. The fungus infects tissues and blood arteries, interrupting blood supply to normal tissue. As a result of the loss of blood supply, the infected area turns black and necroses, earning the term black fungus ¹.

History: Mucormycosis is normally rare, affecting less than 2% of the population in San Francisco,

each year, but it is currently 80 times more common in India. People of all ages, including premature infants, may be impacted. Friedrich Küchenmeister may have described the first instance of Mucormycosis in 1855. Natural calamities such as the 2004 Indian Ocean tsunami and the 2011 Missouri tornado earthquake have been linked to the disease. A link between Mucormycosis and COVID-19 was discovered during the COVID-19 epidemic in 2020/21. Reduced immunological function and glucocorticoid medication during Covid-19 are linked to this relationship ².

Classification: Mucormycosis is divided into six categories based on the portion of the body that is affected:

- ❖ Sinuses and brain (rhinocerebral).
- ❖ Lungs (pulmonary).
- ❖ The intestines and stomach (gastrointestinal).

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- ❖ The skin (cutaneous).
- ❖ Widespread (disseminated) when an infection spreads through the bloodstream to other organs.
- ❖ Kidney mucormycosis.
- ❖ Epidemiology.

Mucor is found in 0.14 per 1000 people in India, which is 80 times more than in developed countries. Mucormycosis has a 46 percent fatality rate worldwide. So, far, 11,717 instances of black fungus have been reported in India. In Kerala, 45 instances have been documented. Rhino orbito cerebral Mucormycosis is the most prevalent type of Mucormycosis, which affects the nose, eye, and brain (ROCM). As incidences of the fatal uncommon infection rise among patients recuperating from Covid-19, states across India are labelling it a pandemic. Mucormycosis is normally a rare condition; however, it has been documented in more than 7,200 patients in India, with 219 deaths³.

Causes of Mucormycosis: The invasion of the Rhizopus and Mucor genera, which are common bread moulds, is the most common cause. Rhizopusoryzae is responsible for the majority of deadly infections. It's less likely to be caused by Lichtheimia and only very rarely by Apophysomyces.

When the fungus is deposited, it produces branch-like filaments that infiltrate blood vessels, causing clots to form and surrounding tissues to perish.

Patients who are recuperating or have recovered from COVID-19 have been found to have the condition. The following diseases in COVID-19 patients, according to an advisory given by the Indian Council of Medical Research, enhance the risk of mucormycosis infection.

- Diabetes that is uncontrolled.
- Immune system deterioration as a result of steroid use.
- A stay in the intensive care unit (ICU) or in the hospital for an extended period of time.
- Co-morbidities/post-transplantation/cancer.
- Voriconazole treatment (used to treat serious fungal infections).

It is not passed on from person to person. As a result, it was not communicable. Diabetes with chronically high blood sugar levels or diabetic ketoacidosis, low white blood cells, cancer, organ transplant, iron overload, kidney issues and long-term use of steroids or immunosuppressants are all risk factors⁴.

Relation with COVID-19: Mucormycosis is caused by a group of microorganisms called mucormycetes, which are found in nature, primarily in soil and decomposing organic materials. In general, our bodies' immune systems battle fungal infections successfully.

COVID-19, on the other hand, has an effect on our immune system and its therapy entails the injection of medications such as dexamethasone, which suppresses our immune system's response. Furthermore, COVID patients receiving oxygen therapy in an ICU with a humidifier are susceptible to fungal infection due to moisture exposure.

As a result of these circumstances, they are once again at risk of succumbing to attacks by organisms such as mucormycetes⁵. However, this does not mean that Mucormycosis will infect every Covid patient.

Although the disease is rare in people who do not have diabetes, it can be fatal if not treated promptly. Early diagnosis and treatment are critical for a successful recovery.

Common Symptoms: The signs and symptoms of Mucormycosis vary depending on where the infection is located in the body. Infection usually starts in the mouth or nose and spreads to the eyes, where it reaches the central nervous system.

Mucormycosis begins as a skin infection in the air pockets behind our eyes, nose, cheekbones, and in the space between our eyes and teeth.

It then spreads to the eyes, lungs, and possibly the brain. It causes nose darkening or blackening, impaired or double vision, chest pain, breathing difficulty and bloody coughing.

Due to tissue loss, the affected skin may look like a darkish reddish sensitive patch with a deepening center⁶.



FIG. 1: BLACK FUNGUS

Prevention & Treatment: The infection starts as a skin infection and then spreads throughout the body. Surgical removal of all dead and contaminated tissue results in the loss of the upper jaw and eye. Intravenous antifungal medication is used for a period of 4-6 weeks. One of the most important preventive approaches advised by the ICMR is diabetes control. As a result, diabetic Covid-19 patients must exercise extreme caution. Self-medication and steroid overdosage can have grave consequences; thus doctors' orders should be strictly observed. In the early stages of Covid-19, steroids should never be used. Only after the sixth day of infection should be taken. To avoid negative drug side effects, ensure that drugs are used rationally⁷.

In its guidelines, the ICMR urged COVID-19 patients to stop taking immunomodulating medications. The National COVID-19 Task Force has altered tocilizumab's dosage to avoid side effects. Maintaining good hygiene might also aid in the prevention of a fungal infection. The water in the humidifier should be clean and refreshed regularly for patients on oxygen therapy. Water leaks should be avoided at all costs (to avoid damp surfaces where the fungus can thrive)⁸. After healing from COVID-19, it is important to keep a close eye on any warning signs and symptoms, as the fungus infection can resurface weeks or months later. The treatment includes an intravenous infusion of normal saline (IV) followed by an infusion of Amphotericin-B and antifungal therapy for at least 4-6 weeks to maintain appropriate systemic hydration. Fever, headache, coughing, shortness of breath, bloody vomit, and changed mental status are all warning indications of pain and redness around the eyes or nose.

- ❖ Sinusitis - nasal blockage or congestion, nasal discharge (blackish/bloody).
- ❖ Local pain on the cheek bone, one-sided facial pain, numbness or swelling.
- ❖ Blackish discoloration across bridge of nose/palate.
- ❖ Loosening of teeth, jaw involvement.
- ❖ Thrombosis, necrosis, septicemia.

Following Covid-19 treatment, it is necessary to control hyperglycemia and monitor blood glucose levels. Steroids should be used with caution – the timing, dose, and duration must all be considered. Mucormycosis can cause the upper jaw and possibly the eye to be lost. Mucormycosis develops when Covid-19 breaks the back of a patient's family, who is just getting over a viral ailment. Patients who have been treated with steroids and other treatments that reduce the body's ability to resist germs and disease are the most prone to Mucormycosis.

Steroids appear to help prevent some of the harm that can occur when the body's immune system goes into overdrive to fight the coronavirus by reducing inflammation in the lungs for Covid-19. However, in both diabetes and non-diabetic Covid-19 patients, they lower immunity and raise blood sugar levels. This loss of immunity is assumed to be the cause of the Mucormycosis outbreaks. Diabetes weakens the immune system, the Corona Virus exacerbates it, and then anti-Covid-19 steroids add gasoline to the fire⁹.

Biopsy and culture are used to make the diagnosis, and medical imaging is used to evaluate the degree

of the disease. Amphotericin B and surgical debridement are the most common treatments. Invasion into blood vessels can cause thrombosis and, as a result, blood flow loss, death of surrounding tissue. Mucormycosis that is widespread (disseminated) usually affects patients who are already sick from other medical conditions, making it difficult to determine which symptoms are attributable to Mucormycosis. The therapy of Mucormycosis necessitates very carefully sugar management. Steroids must be tapered and eventually stopped. If at all feasible, other medicines that weaken immunity should be stopped. A significant aspect of the treatment is surgical excision of all damaged areas and tissue. This can include endoscopic nasal and sinus surgery, bone removal (including the top section of the mouth, various teeth, and the cheekbone), and eye removal. This is done to prevent infection from spreading further. The most often used antifungal is amphotericin B.¹⁰

Risk Factors: Most people are exposed to Mucorales regularly without developing the condition. Mucormycosis is transferred through inhaling, eating contaminated food, or inhaling spores of Mucorales moulds. Mucormycosis is predisposed by conditions that make people less able to fight infection, such as a low neutrophil count or metabolic acidosis.

Poorly controlled diabetes (particularly DKA), organ transplant, iron overload, cancers such as lymphomas, kidney failure, and long-term corticosteroid and immunosuppressive therapy are all risk factors. Corticosteroids are commonly used to treat COVID-19 and reduce the damage caused by the body's own immune system during a coronavirus infection. They suppress the immune system and raise blood sugar levels in both diabetic and non-diabetic patients. Both of these effects are thought to contribute to Mucormycosis cases. The exact mechanism by which diabetics become vulnerable is unknown. In vivo, high sugar levels alone do not allow the fungus to grow, but acidosis does. People who consume a lot of sugar have higher iron levels, which is also known to be a risk factor for developing diabetes Mucormycosis.

Diagnosis: Imaging, such as a CT scan of the lungs and sinuses, is frequently used. Nodules, cavities,

halo signs, pleural effusion, and wedge-shaped shadows on chest CT scans that show the invasion of blood vessels may suggest a fungal infection but do not confirm mucormycosis. A reverse halo sign in a person with blood cancer and a low neutrophil count indicates mucormycosis. India has the world's second-highest diabetes rate. Misuse of steroids to treat Covid-19 as a cause of the mucormycosis epidemic has also been reported in Covid patients who were on ventilators in intensive care units due to their airways being exposed to humidity and moisture. The increase in cases has resulted in a drug shortage. Dermatophytes and keratinophilic fungi can infect the eyes, nails, hair, and especially the skin, causing ringworm and athlete's foot. Candidiasis, also known as thrush, is caused by a fungus called *Candida albicans*, which is found in people who have suppressed or low immunity. This fungus infection typically causes white patches to appear on the affected area. As a result, it is also known as White Fungus. It can harm the mouth, tongue, skin, nails, hair, food pipe, airway, lungs, and vagina¹¹.

Prevention: Because poorly controlled diabetes is the primary cause, strict sugar control is required. Steroids and antibiotics, in particular, should not be taken without first consulting a doctor.

- Avoid construction sites and damp rooms, as well as cleaning carpets or air conditioning systems.
- Surgical masks should never be reused. • Cloth masks should be washed and sundried properly with bleach and detergent. If the N95 mask needs to be reused, it should be done so at least 5-7 days after the first use, and it should be sundried in between uses.
- Recovered Patients taking Covid should see a doctor if they experience facial pain, headaches, nasal blockage, or eye pain and redness.

Yellow Fungus: Fungal infections have become more common in India, particularly among patients who have just recovered from COVID-19. The first instance of yellow fungus has been recorded in Ghaziabad, Uttar Pradesh. Because this illness causes significant inside harm, yellow fungus must

be treated very away. Mucor septic is another name for a fungus that spreads through contaminated settings or inhaled moulds that thrive in the environment. The transmission of the virus is aided by unsanitary circumstances, inadequate hygiene, and a high amount of humidity. It is not contagious and cannot be passed from one person to another. It differs from black fungus and white fungus infections in that it spreads internally, causing more

harm to internal organs and altering important organ function; hence, it is considered more dangerous, whereas black fungus spreads with characteristic facial disfiguration.

Yellow is the colour of pus, which forms when a bacterial infection occurs. It doesn't mean there's a "new yellow fungus that's more hazardous than black and white fungus"¹².



FIG. 2: YELLOW FUNGUS

Symptoms: Weight loss, tiredness, anorexia (lack of appetite), pus development and leaking, and sunken eyes are among them. Because of the fungal infection, wound healing is slowed and extended. Malnutrition, organ failure, and necrosis may result in severe cases. If the symptoms are not noticed early enough, they may develop more seriously. When the yellow fungus is caught early enough, it can be easily cured.

Risk Factors: It might be a primary or secondary infection depending on the individual's health and risk factors. So far, it's been shown that those with weakened immune systems and pre-existing illnesses like high cholesterol and uncontrolled diabetes are more likely to become infected.

Fungal infections have been observed in people who have recovered from COVID-19:

- Individuals who were on oxygen for a long time.
- Individuals who were in the ICU for a long time.
- Organ transplant recently and have low WBC or immune complications.
- Steroid or antibacterial use for a long time.
- Kidney damage.

Prevention: Because the yellow fungus is such a novel ailment, there isn't much knowledge on it yet. It is, however, preferable to safeguard your health by adopting cautious precautions. Individuals with weakened immune systems and other pre-existing disorders are more susceptible to fungal infections. Diabetes patients should keep their blood sugar levels under control.

They should also maintain hygienic and sanitary conditions in their surroundings. Ensure that all surfaces are disinfected. Individuals should monitor the humidity levels in their rooms and homes. Individuals who require oxygen should ensure that the oxygen is properly filtered and that the water filters are clean and changed regularly. Medication and steroid use should be maintained to a minimum. Doctors also advise that people avoid potentially dangerous surroundings, wear masks regularly and practice social distancing. Amphotericin-B injections can be used to treat it. The key to preventing fungal diseases is cleanliness; the environment should be mold-free. Steroids are lifesavers in the current circumstances, amid the growing pandemic. However, they must be used in little amounts for a short period of time. Antibiotics should be avoided to the greatest extent

possible. COVID is a viral infection, not a bacterial one. Antibacterial medications will only affect the healthy bacteria in the gut if they are used in COVID treatment. The best recipe for fungal infections in individuals is diabetes combined with an overdose of steroids and antibiotics. The primary goal is prevention, which will necessitate a strong immune system, particularly in the post-Covid era.

Does The Color of Fungal Infection Matter: The words 'Black Fungus,' 'White Fungus,' and 'Yellow Fungus,' for example, might be misleading and cause alarm. Instead of focusing on the colour, it's vital to examine the infection, the causes for its occurrence, and the risk factor. In the second wave, the use of steroids has grown, which lowers a person's immunity and makes them more vulnerable to infection and increased usage of industrial oxygen. When the fungus enters a person through their lungs or through contaminated food, they get infected. It can be fatal for persons who have a weak immune system. Because fungi cannot be passed from person to person, they are not contagious. However, it is crucial to note that the majority of fungal infections of this type begin as a

result of unsanitary settings such as inadequate hygiene, contaminated food, or abuse of steroids or antibacterial drugs¹³.

White Fungus: Because the white fungus spreads, it can harm key organs, making it more fatal. The brain, digestive system, respiratory organs, kidneys, and even private areas are all affected. *Candida* is a yeast genus that includes white fungus. They develop on the mucosa of the oral cavity in humans as white, creamy patches. They are found in the mouth cavity and gastrointestinal tract, as well as on the skin. The most usually isolated species is *Candida albicans*. *Albicans* is a Latin word that means "white." As a result, the term "white fungus" was coined.

Candida fungi are divided into *auris* and *albicans*, both of which can be lethal to humans. Another type of fungus, *Aspergillus*, causes death by infecting the lungs. *Candida* and *Aspergillus* are the two most common fungi that kill people. *Candida* is a bacterium that can be found on a variety of surfaces, including shower curtains, computer displays, doctor's stethoscopes, and train carriage railings¹⁴.

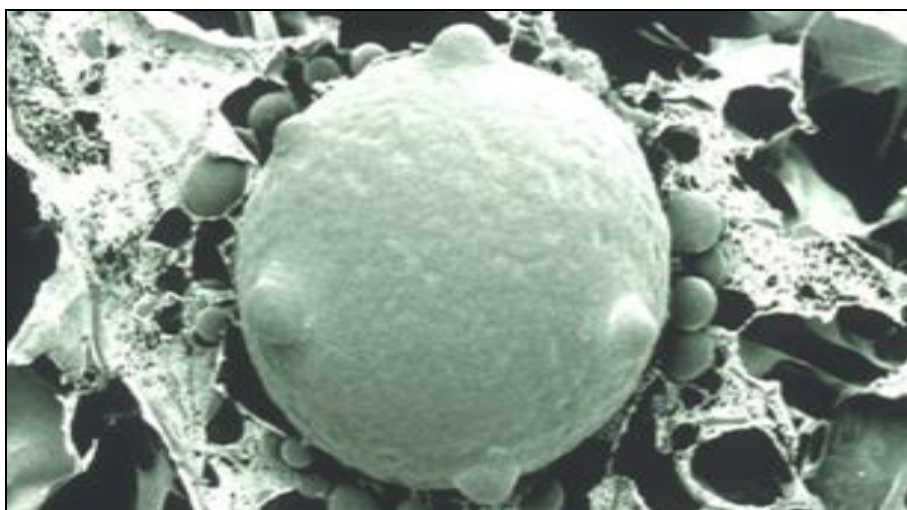


FIG. 3: WHITE FUNGUS

Symptoms: Fever, coughing, and shortness of breath are all frequent symptoms. White-colored thrush in the nose, mouth, lungs, and stomach, as well as nail beds, are indications of superficial *Candida* infections, hence the name "white fungus." Hypotension, fever, stomach pain, and UTI indicate a more invasive kind of infection, which occurs when the insect enters the bloodstream.

Causes: Overuse of steroids and other medicines weakens the immune system and exacerbates underlying illnesses, making Covid-19 patients in critical care more vulnerable to infections. It's almost as if you're waging a lost war. A single antifungal medicine called Amphotericin B is used to treat all fungal infections in the country.

CONCLUSION: Mucormycosis is the cause of all of these fungal illnesses. The fungus is known as 'Black Fungus' when it infects the nose, face, orbits of the eyes, brain, and lungs, causing the tissues to turn black. The name "white fungus" comes from the white discharge that occurs when a fungus infects private regions.

The fungus was given the name "yellow fungus" because of the yellow pus that it produces when it infects a region. It is more important to define these infections based on the colour of the discharge or the appearance of the affected body area. In most circumstances, people with high glucose levels are at high risk of fungal infection.

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REFERENCES:

1. Mehta S and Pandey A: Rhino-orbital mucormycosis associated with COVID-19. *Cureus* 2020; 12.

2. Mishra N, Mutya VSS and Thomas A: A case series of invasive mucormycosis in patients with COVID-19 infection. *Int J Otorhinolaryngol Head Neck Surg* 2021; 7(5): 867–870.
3. Benoit Pilimis: Recent advances in the understanding and management of mucormycosis. *F1000 Res* 2018; 7: 1429.
4. Suganya Ramalingam: Mucormycosis: A Brief Review *J Pure Appl Microbiol* 2019; 13(1): 161-165.
5. Anna Skiada: Epidemiology and Diagnosis of Mucormycosis: An Update *Journal of Fungi* 2020; 6: 265.
6. Millon L: Molecular Strategies to Diagnose Mucormycosis. *J Fungi* 2019; 5: 24.
7. Hariprasath Prakash: Epidemiology of Mucormycosis in India. *Microorganisms* 2021; 9: 523.
8. Son HJ: A comparison of histomorphologic diagnosis with culture- and immunohistochemistry-based diagnosis of invasive aspergillosis and mucormycosis. *Infect Dis* 2020; 52: 279–283.
9. Anna Skiada: Epidemiology and Diagnosis of Mucormycosis: An Update. *J Fungus* 2020; 6: 265.
10. Deepak Garg: Coronavirus Disease (Covid-19) Associated Mucormycosis (CAM): Case Report and Systematic Review of Literature. *Mycopathol* 2021; 186: 289–298.
11. Guegan: Evaluation of Mucor Genius mucorales PCR assay for the diagnosis of pulmonary mucormycosis. *J Infect* 2020; 81: 311–317.
12. Brad spellberg: Novel Perspectives on Mucormycosis: Pathophysiology, Presentation and Management. *ASM* 2020; 8: 3.
13. Garg D: Coronavirus disease (Covid-19) associated mucormycosis (CAM): case report and systematic review of literature. *Mycopathologia* 2021; 186(2): 289–298.
14. Chander J: Mucormycosis: battle with the deadly enemy over a five-year period in India. *J Fungi* 2018; 4(2): 46.

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